Title of Thesis	**SYNTHESIS AND ANTIMICROBIAL ACTIVITY OF SOME HYDROXAMIC ACIDS**
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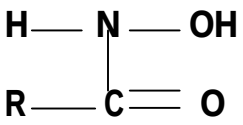
SYNTHESIS AND ANTIMICROBIAL ACTIVITY OF SOME HYDROXAMIC ACIDS

1. INTRODUCTION:-

When hydroxylamine is inserted in to carboxylic acid with R, the new compound is formed known as hydroxamic acid. The chemical formula of hydroxamic acid and their derivatives is RC (= O) NHOH and RC (= O) NR'OH where 'R' & R' as an organic residue i. e. alkyl, aryl & heterocyclic ring, a >CO as a carbonyl group, and a hydroxylamine as NH_2OH.



General Structure of Hydroxamic acids

Hydroxamic acid is first discovered by Walroos and Virtanen [1] in 1959, oxyhydroxamic acid is discovered by H. Lossen in 1869[2], but first study of this compound is started from 1980 due to pioneering study of Tandon[3], Exner, Raymond, Crumbliss, and Farkas. One of the most important properties of hydroxamic acid is contain hetero atom on their carboxylic ring knows as heterocyclic hydroxamic acid.

First synthesis of hydroxamic acid by acylation of hydroxylamines by ester, acid anhydrides or acid chloride[4]. Bamberger[5] was developed formation of N-substituted hydroxamic acid by acylation of N-substituted hydroxylamine in presence of base later on different method for the preparation of hydroxamic acid[6]. One standard method adopted by Priyadarshini and Tandon has been mainly used for the synthesis of various unsubstituted N – monosubsituted and N- benzyl hydroxamic acids.

High applicability of hydroxamic acid in divers' field [7-8] works on acid base equilibrium and, complexation with metal ions have come in trend in various laboratories. Many works has done on acid catalyze hydrolysis of different mono, di, and tri hydroxamic acid [9-10] but scare literature is available on hydroxamic acids. It was through worthwhile to investigate the kinetic and mechanism of acid catalyzed hydrolysis of hydroxamic acids.

Increases utility of analytical reagent, hydroxamic acid use as chelating agent because hydroxamic acid having ability to formation of metal complex, by chelating, of metal ion

between the two oxygen atom of the mono anion to give five member ring. Hydroxamic acid has also having ability to formation of stable transition metal complexes which are soluble or insoluble coloured complex.

The rising prevalence of multi-drug resistance of bacteria, fungi, virus and algae continues to provide impetus for the search and discovery of novel antimicrobial agent active against these pathogens [11].

Hydroxamic acids are a novel class of totally synthetic antimicrobial agent active against some bacteria, fungi, virus, and algae are actively use as antibiotics, antibacterial, antitumor[12-13], antifungal[14-15], anti-inflammatory[16-17] and anticancer agents[18]. Hydroxamic acids are reacting with both protein and nucleic acids [19].

One of the most important activities to inhibit various enzyme & maintenance of enzyme conformation, like peroxidase [20], ureases [21] or ribonucleotide reductase, metalloproteinase [22-23], thermolysin, elastase, amino peptidase of enzyme inhibition for hydroxamic acids by electrophilicity allows the molecule to react with nucleophilic centre present in enzyme involved in fundamental process.

It is well known from the literature that the some hydroxamic acids are well established as effective inhibitors of plants and bacterial urease in vitro and have been shown to effectively inhibit ureolytic activity and lower blood ammonia levels in mice, rate, sheep, cows, dogs , and men.

The potential application of hydroxamic acids in treatment of various disease viz- hepatic coma & in the improvement of nitrogen utilization by ruminant animals has led to the present series of their physiological deposition in the animal body, HIV-1, bone marrow, ehrlirch ascitescarcinoma cell (EAC), thalassaemia major [24], cooley's anemia etc.

The chemical interaction of plants within the same species or between plants of different species is important in the plant competition for water, nutrients and light. Hydroxamic acids have been ascribed a role in this interaction in many reports.

Hydroxamic acids have been shown to have a negative impact on the survival and reproduction of aphides but scare literature is available on some hydroxamic acids.

2. A brief review of the work already done in the field:-

There are various studies reported on particulate matter in India and over the world and very few data available on the **"Synthesis And Antimicrobial Activity of Some Hydroxamic Acids".**

Jan et al (1997)[25] have synthesized a number of monohydroxamic acid like salicyl, cinnamo, m-nitro, tartaric and benzo hydroxamic acid , and dihydroxamic acid were synthesized and characterized using spectroscopic techniques and developed selective agents for determination of transition metal like Mn(II), Co(II), Pd(II), Cu(III), V(V) and Mo(VI).

Hackbarth et al (2002)[26] have identified N-alkyl urea hydroxamic acid as a new class of PDF (peptide deformylase) enzyme inhibitors. This class of compounds has potent whole- cell activity against both, some gram positive and negative bacteria. Gupta et al (2002)[27] reported that β-sulfonyl and β-sulfonyl derivatives of hydroxamic acid and also reported that PDF (peptide deformylase) enzyme inhibition activity in some bacterial cell.
Sosa et al (2005)[28] have also reported that inhibion of both, some gram positive and gram negative bacteria by the N-phthaloylamino hydroxamates inhibition of probably the most important enzyme for the growth of bacteria the PDF (peptide deformylase) enzyme.

Pepeljnak et al (2005)[29] have reported that hydroxamic and polyhydroxamic acid showed a narrow spectrum of antimicrobial activity and also reported polyhydroxamic acids caused hemolysis of the blood agar and they cannot be used in antimicrobial therapy of humans this compound could be possible used in disinfection but at higher concentration.

Agrawal et al (2010)[30] have synthesized certain type of hydroxamic acid and characterized on the basis of ^{1}HNMR, ^{13}CNMR, and IR spectral data all compounds were founds to be potential bioactive against the some pathogenic microorganism.

Jahangirian et al (2011)[31] have also synthesized deferent type of hydroxamic acid. Kushwaha et al (2011)[32] have synthesized certain hydroxamic acid and also reported that antimicrobial activities against some gram positive and negative bacteria in vitro. Jahangirian et al (2011)[33] have synthesized phenyl fatty hydroxamic acid and also reported that antibacterial activity against some bacterial species.

3. OBJECTIVE:-

I. To explore the characteristic of an interaction between the hydroxylamine and cinnamoylchloride.

II. Synthesis of some cinnamoyl hydroxamic acids and their derivatives.

III. Characteristics study of cinnamoyl hydroxamic acids by ^{1}HNMR & IR spectrum.

IV. Spectrophotometric analysis of vanadium in soil sample, biological sample, pharmaceutical sample, and different steel samples.

V. Investigation of antimicrobial activity of cinnamoyl hydroxamic acids against some bacterial and some fungal species.

4. Noteworthy contribution in the field of proposed work (Synthesis and Characterization, Antimicrobial properties):-

Continuous to use one type of antimicrobial agent, bacteria and fungi have develop resistivity against this antimicrobial agent so that it is necessary to use new type of antimicrobial agent many investigators have focused their experiments to the synthesis of hydroxamic acid but scare literature is available on antimicrobial activity of hydroxamic acid.

Raghawan et al (2007) [34] have reported that synthesis, kinetics and biological activity of some synthesized (some furo derivatives) heterocyclic hydroxamic acid against some bacterial and fungal species.

Shekhawat et al (2012)[35] have also reported that synthesis, kinetics and biological activity of some synthesized (some thio derivatives) heterocyclic hydroxamic acids against some bacterial and fungal species

Krishnan et al (2013)[36] have also reported that synthesis, kinetics and biological activity of some synthesized (some furo derivatives) heterocyclic hydroxamic acids against some bacterial and fungal species

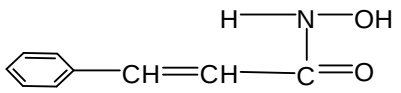
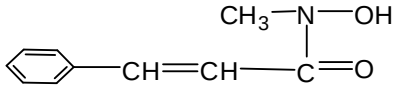
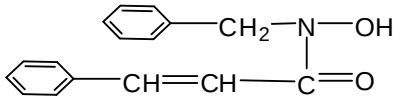
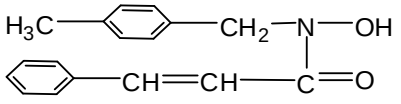
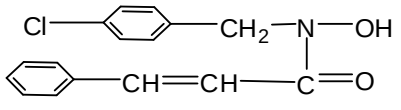
5. Proposed methodology:-

Several methods will have use for our present investigation

(I) Various methods for synthesis of hydroxamic acid are known but one standard method adopted by Priyadarshini and Tandon have used for the synthesis of various unsubstituted N-mono substituted and N-benzyl hydroxamic acid we will use this methods for synthesis of cinnamoyl hydroxamic acids and their derivatives.

(II) All the physico-chemical properties of this cinnamoyl hydroxamic acid will have study by their melting point determination and characterization by elemental analysis ^{1}HNMR and IR spectrum.

We will synthesize and characterize following cinnamoyl hydroxamic acids:-

S.NO.	HYDROXAMIC ACID	TRIVIAL NAME	STRUCTURE
1.	Cinnamoyl hydroxamic acid	CHA	
2.	N-methyl cinnamoyl hydroxamic acid	MCHA	
3.	N-benzyl cinnamoyl hydroxamic acid	N-BCHA	
4.	N-p-methyl benzyl cinnamoyl hydroxamic acid	p-CH_3BCHA	
5.	N-p-Chloro benzyl cinnamoyl hydroxamic acid	p-ClBCHA	

(III)Spectrophotometric determination of Vanadium:- Simple rapid and sensitive spectrophotometric methods will have use for determination of vanadium using some synthesized cinnamoyl hydroxamic acid. The method is based on the formation of purple coloured complexation reaction of vanadium (v) with synthesized hydroxamic acid in 3M hydrochloric acidic medium at pH 2.6 with using Beer' s law. Now further continue our work with determination of vanadium in different sample by use of spectrophotometric methods:-

a) Determination of vanadium in soil sample.
b) Determination of vanadium in biological sample.
c) Determination of vanadium in pharmaceutical sample.
d) Determination of vanadium in different steel sample.

VI) For the study of antimicrobial activityof some newly synthesized cinnamoyl hydroxamic acid, following method will have apply:-

A)Paper Disc Agar plates method: - A susceptible culture of different bacteria (*Xanthomonas citri, Xanthomonas oryzae, Pseudomonas solenaciraum*) and fungus *(Penicillium, Fusarium, Alterneria alternata*) will have grow on NAM and PDA of the specified composition for some days and test solution of different concentration will have prepare and diffuse in petriplates containing NAM, PDA media and now bacterial loops and fungal needle will have inoculate at the centre of plates with the help of inoculating needle and plates will have placed in incubator, control plates will have also place in inoculating chambers. The percentage inhibition in colony of the test bacterial and fungal will have calculated with following equation:-

$$\% \text{ Inhibition} = \frac{(C-T) \times 100}{C}$$

Where,
C= Diameter of fungus colony (mm) in controls plates.

T= Diameter of fungus colony (mm) in test plates

Order of plan of work

I. Introduction.

II. Synthesis and characterization of cinnamoyl hydroxamic acids by ^{1}HNMR and IR.

III. Experimental section..

IV. Facil and sensitive spectrophotometric determination of vanadium.

V. Antimicrobial activity of some cinnamoyl hydroxamic acid against some bacterial & fungal species.

6. Outcomes of the Proposed work:-

1. Chemistry of some newly designed cinnamoyl hydroxamic acids.

2. Broad application of some synthesized cinnamoyl hydroxamic acids.

3. Understanding the study of synthesized cinnamoyl hydroxamic acids are play important role in the fields of kinetics.

4. Understanding the metal complexation behavior of synthesized cinnamoyl hydroxamic acids may prove to be advantageous compounds in pharmaceutical and medicinal field.

5. Find out the synthesized compounds having better antibacterial and the antifungal properties.

6. Understanding the synthesized compounds exhibited better antibacterial activity than reference standard antibiotic against the some bacterial & fungal species.

7. Expected methods are simple and very sensitive in every field.

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8. List of Contributions:-

Paper presentation

1. 31st conference of Indian council of chemists department of chemistry Saurashtra University Rajkot on 26th-28th December 2012, on "Design synthesis kinetics and antimicrobial activity of some heterocyclic hydroxamic acids."

Seminar

1. National seminar "Changing environment and its impact on biodiversity" 11-12 October, 2012, organized by department of botany Govt. D. B. Girls P. G. Autonomous College Raipur (C.G.).

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